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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 17

Serial Number: 08/013871
Filing Date: 1/27/98
Appellant(s): Martin et al.

Allan P. Halluin
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's Brief on appeal filed 5/18/01 (Paper No. 16).

The text of those sections of Title 35 U.S. Code not included in this appeal can be found in a previous Office Action herein.

(1) Real Party of Interest.

A statement identifying the real party of interest in contained in the Brief.

(2) Related Appeals and Interferences Identified.

A statement identifying that no related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the Brief.

(3) Status of Claims.

The statement of the status of claims contained in the Brief is incorrect.

A correct statement of the status of the claims is as follows:

Upon reconsideration, including appellant's statements in the Brief, filed 5/18/01 (Paper No. 16) that the recitation of "Dreg55", "HuDreg55" and "HuDreg200" refer to specific antibodies; the previous rejection of claims 27, 40 and 44 under 35 U.S.C. § 112, second paragraph, has been withdrawn.

It should be pointed out that "HuDreg200" is a humanized antibody and not a mouse monoclonal antibody, as indicated on page 7, line 2 of appellant's Brief.

Also, it should be pointed out that page 7, lines 6-7 of appellant's Brief should be read as "and would not be interpreted as any other molecules or matter" rather than "and would be interpreted as any other molecules or matter", as currently indicated.

The statement of the status of claims contained in the Brief is correct with respect to the rejections under 35 U.S.C. § 102(b)(e) and § 103(a).

This appeal involves claims 22, 23, 27, 29-45.

(4) Status of Amendments After Final.

The appellant's statement of the status of amendments after final rejection contained in the Brief is correct.

(5) Summary of Invention.

The summary of invention contained in the Brief is correct.

(6) Issues.

The appellant's statement of the issues in the Brief is incorrect.

As pointed out above in Section 3; the previous rejection of claims 27, 40 and 44 under 35 U.S.C. § 112, second paragraph, has been withdrawn.
Therefore , Issue (a) is not in question in the instant application.

(7) Grouping of Claims.

Appellant's Brief includes a statement that claims do not stand or fall together and provides reasons in the Arguments (Section 8 of appellant's Brief), as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed.

The copy of the appealed claims contained in the Appendix to the Brief is correct.

(9) Art of Record.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

A) Buerke et al.; J. Pharmacology and Experimental Therapeutics 271: 134-142 (1994).
B) Butcher et al.; U.S. Patent No. 5,316,913.
C) Co; WO 94/12215.
D) Finn et al.; Perfusion 8: 39-48 (1993).
E) Lefer; WO 95/95181.
F) Moat et al.; Ann. Thorac. Surg. 56: 1509 - 1541 (1993).
G) Springer et al.; U.S. Patent No. 5,460,945.
H) Tedder et al.; U.S. Patent No. 5,679,346.

(10) Grounds of Rejection.

The following ground(s) of rejection are applicable to the appealed claims.

Rejection Under 35 U.S.C. § 102(b)

Claims 22, 23, 27, 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Co (WO 94/12215). Co teaches the use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

Rejection Under 35 U.S.C. § 102(b)

Claims 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lefer (WO 95/95181). Lefer teaches the use of humanized DREG 200 to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. ischemic events, cardiac surgery, angioplasty, multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with L-selectin-specific antibodies.

Rejection Under 35 U.S.C. § 102(e)

Claims 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Tedder et al. (U.S. Patent No. 5,679,346). Tedder et al. teach the use of LAM-1-specific antibodies including recombinant antibodies thereof to inhibit a number of disorders or conditions encompassed by the claimed methods (e.g. neutrophil-mediated inflammation, reperfusion injury and multi-organ failure) (see entire document, including columns 6-7, overlapping paragraph). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations addressed by the applicant would be inherent properties of the referenced methods with LAM-1-specific antibodies. The LAM-1 specificity is the same as the L-selectin specificity.

Rejection Under 35 U.S.C. § 103(a)

Claims 22, 23, 27 and 29-45 stand rejected under 35 U.S.C. § 103 as being unpatentable over Co (WO 94/12215) AND/OR Lefer (WO 95/1515181) AND/OR Tedder et al. (U.S. Patent No.5,679,346 5,679) AND/OR Buerke et al. (J. Pharmacology and Experimental Therapeutics 271: 134-142, 1994) in view of Butcher et al. (U.S. Patent No. 5,316,913), Springer et al. (U.S. Patent No. 5,460,945), Moat et al. Ann. Thorac. Surg., 1993; 1449), Finn et al. (Perfusion, 1993). The instant claims are drawn to using L-selectin-specific antibodies in the treatment of polytraumatic events and extracorporeal circulation.

Co teaches the use of humanized DREG 55 and DREG 200 antibodies to inhibit inflammatory disorders including the conditions encompassed by the claimed methods and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Methods of Use).

Lefer teaches the use of humanized DREG 200 to inhibit a number of disorders associated with reperfusion-ischemia including the conditions encompassed by the claimed methods and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods).

Buerke et al. (J. Pharmacology and Experimental Therapeutics, 1994) teach the use of humanized DREG 200 to protect from myocardial reperfusion injury and the importance of blocking neutrophil-endothelial interactions and protecting cardiac function against necrotic tissue injury (see entire document). Buerke et al. also acknowledges that this protection may occur by inhibition of neutrophil rolling along the endothelium, thereby inhibiting subsequent tight neutrophil adhesion and release of mediators with their known exacerbation (see Discussion, particularly page 141, column 1, paragraph 2). Therefore, there was expectation of success of L-selectin inhibitors in view of neutrophils shedding L-selectin upon activation. Buerke et al. differs from the instant methods by not disclosing extracorporeal circulation and polytraumatic event per se, however in treating the reperfusion injury targeted by Buerke, it would have been obvious to treat similar conditions associated with extracorporeal circulation and traumatic events that would benefit from the inhibition of neutrophil-endothelial interactions.

Tedder et al. teach the use of L-selectin-specific antibodies in the amelioration of inflammatory conditions including those encompassed by the claimed methods (see entire document, including Methods of Use and Use). These references differ from the instant methods by not disclosing the DREG 55 and DREG 200 specificity per se.

Butcher et al. teach neutrophil L-selectin as a indicator of neutrophil activation and that DREG 55 and DREG200 were known in the prior art (see entire document, including column 5, lines 21-24).

Springer et al. teach the use of inhibitors of neutrophil-endothelial interactions such as L-selectin antagonists (column 13, lines 42-57) including targeting the therapeutic endpoints encompassed by the instant methods (see entire document, including column 30 Section 5.11).

Moat et al. and Finn et al. teach the role of neutrophil adhesion and activation in cardiopulmonary bypass and the importance of blocking said function. As Buerke et al. points out; L-selectin-mediated inhibition confers protection in reperfusion injuries and this may occur via inhibition of neutrophil rolling along the endothelium, thereby inhibiting subsequent tight neutrophil adhesion and release of mediators with their known exacerbation.

Co, Lefer, Buerke et al. and Tedder et al. differ from the instant claimed methods by not disclosing all of the time points for administering the inhibitory L-selectin antibodies, however dosages and administration would rely upon the needs of the patient and the nature of the intended therapeutic endpoint. Co and Lefer do teach single and multiple administrations sufficient to cure or at least partially arrest the disease and its complications; which would depend on the severity of the disease and general state of the of the immune system in a patient; which can be administered as bolus or repeated injections to achieve optimal plasma levels of antibody and alone or in combination with other therapeutic agents or drugs (see Methods of Use). Also, the ordinary artisan would have expected to reduce the probability of organ failure after a polytraumatic event, given the teachings of the prior art, including Methods of Use, as taught by Co and Lefer.

Therefore, the prior art made and used L-selectin antibodies including the DREG 55 and DREG 200 specificities to inhibit inflammation including those associated with neutrophil adhesion and activation and the nature of the injuries claimed in the instant methods. The particular humanized L-selectin antibodies were known in the prior art or could have been made by routine technology at the time the invention was made. Although some of the references are silent about the exact sequences of the L-selectin-specific antibodies, the standard recombinant techniques and computer analyses of CDR known in the prior art would have resulted in the same or very nearly the same structural and functional characteristics of the instant claims since both the references and instant invention use the same techniques, the same antibody specificities and the same goals. For example, see the humanization of antibodies taught by Co and Lefer. Also, such humanization of antibodies for therapeutic uses was well known and practiced at the time the invention was made. The claimed functional limitations encompassed by the claims would be expected properties of selecting for L-selectin-specific antibodies to specifically bind and inhibit L-selectin.

The claims drawn to specifically defined humanized antibodies are obvious since the record does not contain any evidence that the antibodies differ in any significant manner that one of ordinary skill in the art would expect to generate using L-selectin as the starting antigen in the basic method of generating antibodies and humanizing said antibodies.

There appears no evidence that the use of various sources of framework amino acids would differ in an unexpected or distinct manner from those available to the ordinary artisan at the time the invention was made. Also, Co and Lefer appear to teach the same DREG 55/DREG 200 antibodies of the claimed invention.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of L-selectin-specific antibodies as a therapeutic regimen in treating cardiovascular and traumatic diseases. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(11) Response to Argument

Rejection Under 35 U.S.C. § 102(b)

Claims 22, 23, 27, 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Co (WO 94/12215).

Appellant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Appellant argues in conjunction with a number of legal decisions that a claim is anticipated only if each and every element as set forth in the claims is found is either expressly or inherently described in a single prior art reference.

Appellant acknowledges that Co disclose prevention and treatment of a variety of injuries, syndromes, disorders and diseases, but asserts that none of these is a polytraumatic event.

Appellant asserts that a polytraumatic event is an event that results in a simultaneously acquired injury of at least two or more organ systems, which is immediately life threatening.

While it has been acknowledged that Co does not disclose the term "polytraumatic" per se; it is noted that it is the term "polytraumatic", particularly the term "poly", that is not disclosed in the prior art.

In contrast to appellant's assertions, Co clearly teach a number of conditions that are encompassed by the claimed methods and therapeutic endpoints.

Appellant has relied upon pages 1-2 of the instant specification for a discussion on severe polytrauma.

Here, the specification as filed discloses that polytrauma is understood as an injury of a number of tissues (bones or soft tissue), which is associated with hemorrhagic shock and that multiple organ failure is a severe problem which occurs after polytrauma.

Appellant again asserts that it is incorrect to think of the claimed invention as an aspect of the treatment of ischemic-reperfusion injury.

Appellant finds not mention in Co of heart/lung machines or any of the conditions (e.g. acute organ damage) elaborated in the claims.

Appellant also attempts to distinguish the prior art from the instant claims by asserting that Co discloses that the ischemia-reperfusion injury after multiple organ failure, while the claimed method is a prophylactic treatment prior to organ failure.

In contrast to appellant's assertions; page 4, paragraph 1 of the specification relies upon the art known association of the selectins (e.g. L-selectin) with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.

Also, the specification as filed acknowledges the art known recognition that acute organ damage occurs after extracorporeal circulation during cardiovascular surgery such as bypass operation where the blood of the patient circulates extra corporeally through a heart-lung machine (e.g. see page 4, paragraph 4 of the specification)

It is noted that appellant acknowledges that a reference anticipates a claimed if it discloses the claimed invention "such that a skilled artisan could take its teachings in combination with his own knowledge of a particular art and be in possession of the invention", citing In re LeGrice.

In contrast to appellant's assertions, Co clearly teaches the use of L-selectin antibodies, including the use of humanized DREG 55 and DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic-reperfusion events, shock, cardiac surgery, coronary bypass surgery, angioplasty, multiple organ failure as well as injuries dues to trauma, burns, and spinal cord damage) and dosages which depend on the patient and therapeutic endpoint , including prophylactic and emergency treatment (pages 30-31 and 34-35) (see entire document, particularly Methods of Use on pages 29-36, particularly page 29, paragraph 1). Therefore, Co does teach conditions such as multiple organ failure and ischemic-reperfusion events associated with cardiovascular surgery as well as injuries (e.g. trauma, burns, and spinal cord injuries) (page 29, paragraph 1), which read on the polytraumatic events encompassed by the claimed methods.

Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately envisage that such patients were on heart-lung machines as standard operating procedures at the time the invention was made and acknowledged as standard procedures in such cardiovascular procedures on page 4, paragraph 4 of the instant specification.

The prior art is employing the same reagents (e.g. L-selectin-specific antibodies) in the same patients (e.g. cardiac surgery, coronary bypass surgery, angioplasty, multiple organ failure) to achieve the same end results (e.g. treatment), as encompassed by the claimed methods, including preventing of multiorgan failure after a polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001). See MPEP 2112-2112.02.

Appellant's arguments are not found persuasive.

Rejection Under 35 U.S.C. § 102(b)

Claims 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lefer (WO 95/95181.

Appellant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Appellant arguments appear to be the same as that set forth above in the Section rejected under 35 U.S.C. § 102(b) as being anticipated by Co (WO 94/12215).

The disclosures of Lefer (WO 95/95181) and Co (WO 94/12215) overlap to a large degree with respect to the use of the same or nearly the same L-selectin-specific antibodies to treat various conditions.

While it has been acknowledged that Lefer does not disclose the term "polytraumatic" per se; it is noted that it is the term "polytraumatic", particularly the term "poly", that is not disclosed in the prior art.

In contrast to appellant's assertions, Lefer clearly teach a number of conditions that are encompassed by the claimed methods and therapeutic endpoints.

Appellant also argues that Lefer does not anticipate a method for preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart lung machine.

Appellant acknowledges that Lefer does teach the prevention or treatment of reperfusion injury in a patient and treating patients suffering from myocardial ischemia.

In contrast to appellant's assertions; page 4, paragraph 1 of the specification relies upon the art known association of the selectins (e.g. L-selectin) with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.

Also, the specification as filed acknowledges the art known recognition that acute organ damage occurs after extracorporeal circulation during cardiovascular surgery such as bypass operation where the blood of the patient circulates extra corporeally through a heart-lung machine (e.g. see page 4, paragraph 4 of the specification)

It is noted that appellant acknowledges that a reference anticipates a claimed if it discloses the claimed invention "such that a skilled artisan could take its teachings in combination with his own knowledge of a particular art and be in possession of the invention", citing In re LeGrice.

In contrast to appellant's assertions, Lefer clearly teaches the use of L-selectin antibodies, including the use of humanized DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic-reperfusion events, shock, cardiac surgery, coronary bypass surgery, angioplasty, multiple organ failure as well as injuries dues to trauma, burns, and spinal cord damage) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly Therapeutic Methods on pages 21-26, particularly page 21, paragraph 3).

In contrast to applicant's assertions, Lefer clearly teaches the use of L-selectin antibodies, including the use of humanized DREG 200 antibodies to inhibit disorders or conditions encompassed by the claimed methods (e.g. ischemic-reperfusion events, cardiac surgery, angioplasty, hemorrhagic shock) (page 21, paragraph 3) and dosages which depend on the patient and therapeutic endpoint, including prophylactic and emergency treatment (pages 23 and 25-26) (see entire document, particularly Therapeutic Methods on pages 21-26). Therefore, Lefer does teach conditions such as hemorrhagic shock and ischemic-reperfusion events associated with cardiovascular surgery which read on the polytraumatic events encompassed by the claimed methods.

Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately envisage that such patients were on heart-lung machines as standard operating procedures.

The prior art is employing the same reagents (e.g. L-selectin-specific antibodies) in the same patients (e.g. ischemia-reperfusion cause by myocardial infarction, cardiac surgery, coronary artery bypass, angioplasty, shock) to achieve the same end results (e.g. treatment), as encompassed by the claimed methods, including preventing of multiorgan failure after a polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001). See MPEP 2112-2112.02.

Appellant's arguments are not found persuasive.

Rejection Under 35 U.S.C. § 102(e)

Claims 29-33, 39, 41-45 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Tedder et al. (U.S. Patent No. 5,679,346).

Appellant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Appellant's arguments are the same as that set forth above in the rejection under 35 U.S.C. § 102(b) with respect to Co (WO 94/12215).

Appellant asserts that Tedder et al. merely disclose a method of treating a human patient suffering from a lymphocyte-mobilizing condition such as from tissue damage, an autoimmune disorder, or cancer or from an organ or tissue transplant as well as human clinical manifestations, including adult respiratory distress syndrome, multi-organ failure and reperfusion injury, which are not polytraumatic events.

While it has been acknowledged that Tedder et al. do not disclose the term "polytraumatic" per se; it is noted that it is the term "polytraumatic", particularly the term "poly", that is not disclosed in the prior art.
In contrast to appellant's assertions, Tedder et al. clearly teach a number of conditions that are encompassed by the claimed methods and therapeutic endpoints.

Appellant also argues that Tedder et al. do not anticipate a method for preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart lung machine

In contrast to applicant's assertions; page 4, paragraph 1 relies upon the art known association of the selections with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.

In contrast to applicant's assertions, Tedder et al. clearly teach the use of L-selectin antibodies, including the use of recombinant/chimeric L-selectin antibodies to inhibit clinical manifestations encompassed by the claimed methods (e.g. reperfusion injury and multiple organ failure) and dosages which depend on the patient and therapeutic endpoint (see entire document, particularly column 6, paragraph 4). Therefore, Tedder et al. do teach conditions such as multiple organ failure and reperfusion injury encompassed by the claimed methods. The prior art is employing the same reagents in the same patients to achieve the same end results as encompassed by the claimed methods.

Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc. 58 USPQ2d 1508 (CAFC 2001). See MPEP 2112-2112.02.

Appellant's arguments are not found persuasive.

Rejection Under 35 U.S.C. § 103(a)

Claims 22, 23, 27 and 29-45 stand rejected under 35 U.S.C. § 103 as being unpatentable over Co (WO 94/12215) AND/OR Lefer (WO 95/1515181) AND/OR Tedder et al. (U.S. Patent No.5,679,346) AND/OR Buerke et al. (J. Pharmacology and Experimental Therapeutics 271: 134-142, 1994) in view of Butcher et al. (U.S. Patent No. 5,316,913), Springer et al. (U.S. Patent No. 5,460,945), Moat et al. (Ann. Thorac. Surg. 56: 1509-1514, 1993), Finn et al. (Perfusion 8: 39-48, 1993).

Appellant's arguments in conjunction with certain legal decisions have been fully considered but are not found convincing essentially for the reasons of record.

Appellant's arguments the examiner's rebuttal are essentially those set forth above with respect to Co (WO 94/12215), Lefer (WO 95/1515181) and Tedder et al. (U.S. Patent No.5,679,346).

Again, it has been acknowledged that the references do not disclose the term "polytraumatic" per se; it is noted that it is the term "polytraumatic", particularly the term "poly", that is not disclosed in the prior art.

Appellant's arguments concerning the prevention of multiorgan failure after a polytraumatic event or a severe polytraumatic event are acknowledged; however the prior art does teach such methods for the reasons herein.

It does not appear that these claimed purposes and intended results of treating polytraumatic events or severe polytraumatic events result in manipulative difference in steps or targeted patient populations and therapeutic endpoints of the prior art methods.

Appellant's assertion of unexpected results and new advantages are acknowledged.

However, the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(c). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Given the clear teachings by Co, Lefer and Tedder et al. (see citations above) to treat a number of conditions, including ischemia-reperfusion, cardiac surgery, coronary artery bypass, angioplasty, shock, multiorgan failure and traumatic injuries, as acknowledged by appellant; there would have a been a reasonable expectation of success of treating or of multiorgan failure after a (severe) polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine.

As pointed out above, Co (pages 30-31 and 34-35) and Lefer (pages 23 and 25-26) do teach providing L-selectin-specific antibodies to meet the needs of the patients, including providing said L-selectin-specific antibodies before, during and after certain conditions or procedures, including surgery and emergencies.

Again, in contrast to appellant's assertions, Co, Lefer and/or Tedder et al. clearly teach a number of conditions that are encompassed by the claimed methods of treating or preventing of multiorgan failure after a polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine.

Further, given the teachings of treating the ischemic-reperfusion events associated with cardiovascular surgery; the ordinary artisan at the time the time the invention was made would immediately envisage that such patients were on heart-lung machines as standard operating procedures at the time the invention was made and acknowledged as standard procedures in such cardiovascular procedures on page 4, paragraph 4 of the instant specification.

Given the clear teachings by Co, Lefer and Tedder et al. to treat a number of conditions, including ischemia-reperfusion, cardiac surgery, coronary artery bypass, angioplasty, shock, multiorgan failure and traumatic injuries, as acknowledged by appellant; there would have a been a reasonable expectation of success of treating or of multiorgan failure after a (severe) polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine.

As pointed out above, Co, Lefer and Tedder et al. do teach providing L-selectin-specific antibodies to meet the needs of the patients, including providing said L-selectin-specific antibodies before, during and after certain conditions or procedures, including surgery and emergencies (e.g., see Methods of Use, Therapeutic Methods).

In a similar or consistent fashion to the prior art teachings of treating before, during and after surgery and emergencies; it is noted that appellant acknowledges that pages 9-10 of the specification discloses treating patients very soon after the polytrauma to prevent multiple organ failure.

This disclosure of treating very soon after the polytrauma to prevent multiple organ failure is consistent with the prior art teachings and is not consistent with appellant's asserted distinction in preventing multiple organ failure between the instant methods and the prior art methods.

In contrast to appellant's assertions; page 4, paragraph 1 of the specification relies upon the art known association of the selections with tissue damage during the course of ischemic and reperfusion and applicant Examples rely upon ischemia-reperfusion injuries as models of polytraumatic organ failure.

Also, the specification as filed acknowledges the art known recognition that acute organ damage occurs after extracorporeal circulation during cardiovascular surgery such as bypass operation where the blood of the patient circulates extra corporeally through a heart-lung machine (e.g. see page 4, paragraph 4 of the specification)

It is noted that appellant acknowledges that a reference anticipates a claimed if it discloses the claimed invention "such that a skilled artisan could take its teachings in combination with his own knowledge of a particular art and be in possession of the invention", citing In re LeGrice.

Again, it does not appear that these claimed purposes and intended results of treating polytraumatic events or severe polytraumatic events result in manipulative difference in steps or targeted patient populations and therapeutic endpoints of the prior art methods.

In response to appellant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 170 USPQ 209 (CCPA 1971). See MPEP 2145.

Appellant states the secondary references do no remedy the failings of the primary references.

Appellant acknowledges that Buerke et al. teach that the HuDreg200 L-selectin antibody was an effective means to preserve the ischemic myocardium from reperfusion injury.

Appellant acknowledges that Butcher et al. teach methods of determining neutrophil activating in a mammal by detecting LECAM-1 (i.e. L-selectin).

Appellant acknowledges that Moat et al. disclose complement activation, adhesion molecule expression and IL-8 generation in extracorporeal circulation.

Appellant acknowledges that Finn et al. disclose that L-selectin expression was lost in children undergoing cardiopulmonary bypass surgery.

As pointed out previously and herein; Moat et al. and Finn et al. teach the role of neutrophil adhesion and activation in cardiopulmonary bypass and the importance of blocking said function. As Buerke et al. points out; L-selectin-mediated inhibition confers protection in reperfusion injuries and this may occur via inhibition of neutrophil rolling along the endothelium, thereby inhibiting subsequent tight neutrophil adhesion and release of mediators with their known exacerbation.

The prior art is employing the same reagents (e.g. L-selectin-specific antibodies, including the DREG 55 and DREG 200 specificities) in the same patients (e.g. ischemia-reperfusion injury, cardiac surgery, coronary artery bypass, angioplasty, shock) to achieve the same end results (e.g. treatment), as encompassed by the claimed methods and therapeutic endpoints.

Appellant has not provided sufficient objective evidence to support the assertion that the prior art targeted patient populations undergoing cardiovascular surgery, multiorgan failure and trauma do not experience the polytrauma encompassed by the claimed methods.

Again, page 4, paragraph 4 of the specification appears to be consistent with the position that such patient populations were known to undergo (severe) polytrauma and acute organ damage when the blood of the patient circulates extra corporeally through a heart -lung machine.

Again, the prior art, particularly Co and Lefer, teach providing L-selectin-specific antibodies both prophylactically and therapeutically to such targeted patient populations.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of L-selectin-specific antibodies as a therapeutic regimen in treating cardiovascular and traumatic diseases, including preventing of multiorgan failure after a polytraumatic event and/or preventing acute organ damage associated with extracorporeal circulation of a patient's blood through a heart-lung machine. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Appellant's arguments are not found persuasive.

(12) For the above reasons, it is believed that the rejections should be sustained.

Respectively submitted,

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